

**Foundation Fighting Blindness**  
***Insights Forum* Transcript**  
**May 13, 2022**

**Chris Adams, VP, Marketing & Communications:**

Good morning and welcome to the Foundation Fighting Blindness Insights Forum Call. We'll get started in just a few minutes. Thank you.

Good morning. Welcome to the Foundation Fighting Blindness quarterly insights form call I'm Chris Adams, the vice president of marketing communications at the foundation. We appreciate you joining us for today's call. Before we get started, I would like to briefly review a few details for the call. Currently, all participant lines are on listen only mode, with no video. Today's conference is being recorded and is available with closed captioning. To activate the closed captioning, please select the live transcript option located at the bottom of the Zoom interface. Then select 'Show subtitles'. Please note that on today's call our speakers do have their videos live, however, all their comments will be provided verbally, and there are no slides. If you are using a screen reader, please be aware that the controls are at the bottom of the Zoom interface.

The control bar may collapse when it is not in use. If you prefer to prevent the controls from auto hiding, go to the settings within the Zoom platform, select 'Accessibility', and then select 'Always show meeting controls'. It might be helpful to maximize your window and navigate by using the tab key. Additional buttons and settings are available by pressing the alt key. During the call, you may ask questions through the Q and A and chat features, or by sending an in an email to [info@fightingblindness.org](mailto:info@fightingblindness.org). Again, that is [info@fightingblindness.org](mailto:info@fightingblindness.org). We will address questions toward the end of the call during the Q and A session, at which time additional instructions for asking questions will be provided.

I would like to now turn the call over to Jason Menzo.

**Jason Menzo, President and Chief Operating Officer:**

Awesome. Well, thank you so much, Chris. Good morning, everyone. Thank you for joining us today. My name is Jason Menzo. I am the president and chief operating officer here at the Foundation Fighting Blindness. I'd like to take this moment and welcome everyone to our quarterly insights forum webcast. We are very pleased to have you join us today. We've got a lot of updates on a wide range of strategic initiatives here at the Foundation Fighting Blindness. Importantly, we're going to cover a lot of updates with relations to research and development progress within the broader inherited retinal disease community.

We have a very full agenda today with multiple speakers. I'm going to start things off today, actually, talking a little bit about some of our broad organizational updates. We'll highlight one of our most important community engagement activities that occurs every two years, and that is our VISIONS Conference.

After my remarks, our Executive Vice President of Corporate Development and Chief Business Officer, Mr. Peter Ginsberg, will provide a summary of noteworthy fundraising and corporate sponsor initiatives, along with highlights of our financial performance through March 2022. Following Peter, Dr. Amy Laster, who is the Foundation's Vice President of Science and Awards Programs will share details on our new research awards for 2022, including some news hot off the presses. Then our CEO, Dr. Ben Yerxa will highlight several important initiatives and recent gatherings of researchers, funders, and other community members where the foundation played a key leadership role, really on a global scale in some of these initiatives. Then following Ben, we're very excited to have a leading clinician and researcher as our featured guest speaker today, Dr. Mark Pennesi is Professor of Ophthalmology at Oregon Health and Science University, and is also the Chief of the Ophthalmic Genetics Division at the Casey Eye Institute. Dr. Pennesi will discuss the use of gene editing in developing treatments for inherited retinal diseases.

As Chris had mentioned, after our formal remarks, we will have a question and answer period. And at that time, Chris will repeat the instructions on how to ask your questions.

As we mentioned earlier, this call is being closed captioned and a replay and fully accessible transcript will be available on our website in the weeks ahead. Of course, we welcome your feedback, your suggestions related to this webcast, or really anything here at the Foundation Fighting Blindness, in general. You can reach us any time by emailing us at [info@fightingblindness.org](mailto:info@fightingblindness.org). Of course, can learn more about all of these initiatives, upcoming events and the research at our website, which is [fightingblindness.org](http://fightingblindness.org).

Together we're winning. That is our Foundation's tagline and really the perfect sentiment for how things are advancing here in our field. We have so many strategic initiatives underway. Honestly, it's hard to list them all. Sometimes in these calls, we try to list everything that's going on and it becomes kind of like a rundown of so many different initiatives. Today, rather than run down all of the many things that we're working on to improve the activity in the field, I really want to focus on just a few innovative approaches that we're focused on, that are focused on funding that will enable us to significantly expand research, both in the academic and the clinical settings. Today, you're going to hear more about that from Peter and Amy, as it relates to our funding, but also we're focused on partnering. Partnering with other nonprofit and industry organizations, corporate sponsors, investors, legislators, researchers, and of course medical professionals. Ben is going to highlight some of the ways that we're collaborating across our community to accelerate progress on a wide variety of approaches for treatments and cures.

We are working to do all of this with a continually improving efficient operational structure, that's powered by a dedicated staff and volunteers from all across the country, many of you who are on this call here today. One of the key building blocks supporting our ability to win together is our VISIONS Conference. This is a one of a kind biannual event, which takes place every other year. It provides attendees with an opportunity to hear about exciting advancements in research, to gain really practical skills for coping with vision loss, and to learn about products and services that can improve the lives of those who are affected. Also, to connect with others who are blind or visually impaired from across the country. As our first VISIONS Conference since the beginning of the pandemic, this summer's VISIONS 2022, which will be held on June 17th and 18th at Disney's Coronado Springs resort, is going to be very exciting.

We're thrilled to be able to host this conference in-person again, and to share the tremendous progress that has taken place since our last VISIONS Conference, which was way back in 2018. The Foundation funded scientists and researchers in our community are making great progress. We're excited to share all that with you. This conference agenda has been built with a purpose to inspire and to help us all envision the future where we are really winning together to find treatments and cures for inherited retinal disease and dry AMD. Hundreds of individuals in the blind and low vision community are expected to attend VISIONS 2022. Our science-focused programming will cover information on optogenetics, genetic technologies, genetic testing, and counseling through the Foundation's My Retina Tracker registry, cell-based treatments for retinal diseases and clinical trial participation, which is a very common topic, both on these Insights Forums, but also when we receive phone calls and questions from the community. Other sessions will include disease specific clinical updates and sessions on adapting and thriving, including our latest on assistive technology.

We're going to have blind athletes who are breaking barriers, cane safety, and mobility, and how to cope with anxiety, depression, and mental health due to the stress related to vision loss, or those who are serving in a helper role for those who are affected. It really is one of the most comprehensive programs anywhere in the world, serving the blind and low vision community. We're very pleased to welcome all of you to join us next month.

We're going to have a fantastic opening keynote speaker. His name is Chad Foster. Chad is an inspirational change agent who works at Red Hat, which is the entrepreneurial division of the global technology leader, IBM. Chad, despite having retinitis pigmentosa and going blind while attending college in his early twenties, has built a successful career in the technology industry. He was the first blind executive to graduate from Harvard Business School's program for leadership development. He recently published a book that I know many of you are familiar with and probably have read called *Blind Ambition: How to Go From Victim To Visionary*. He's an awesome guy. We're thrilled to have him join us to open VISIONS 2022.

Then we're excited about our closing speaker, which is Dr. Marsha Link. She has a broad range of experience as a clinician, as an executive coach, as an HR professional and as an educator. Marsha has been involved in ophthalmology for many, many years, co-founding a medical device company, and also serving as the President of the Ophthalmic World Leaders or OWL, whose mission is advancing diversity in leadership in the field of ophthalmology.

Marsha is also a co-chair for our Foundation's national capital campaign, which you've all heard much about over the last year, called Victory for Vision. She is personally dedicated to finding cures retinal diseases since one of her family members is personally affected with retinitis pigmentosa. We really look forward to welcoming Marsha to our closing session at VISIONS. She, with her energy, enthusiasm and positive attitude will serve as a fitting closing of the two days that we'll be together next month.

I promise you the VISIONS Conference is truly a one-of-a-kind experience designed specifically for individuals and families who are affected by blinding retinal diseases. I truly hope that each of you will make the opportunity to consider attending VISIONS, this year. Many have already registered, but if you have not, and you are interested, you can find more conference information and sign up to attend at [fightingblindness.org/VISIONS-2022](https://fightingblindness.org/VISIONS-2022). The VISIONS Conference is of course made possible through the dedicated efforts and strong support from our attendees, our staff, our speakers, our volunteer leadership, our exhibitors, and then many, many other people organizations who support this event, in particular are corporate sponsors.

I'm going to turn this call over to Peter Ginsberg, our executive vice president of corporate development and chief business officer to share a little bit more specifically on our relationship with companies and corporate sponsors, not only for VISIONS, but for the foundation's mission in general. Peter, I'll turn the call over to you.

**Peter Ginsberg, EVP, Corporate Development and Chief Business Officer:**

Thanks, Jason. We are so excited about VISIONS. Hard to believe it's just a month away. I want to emphasize the importance of support from our corporate sponsors of the VISIONS Conference. For this year's conference, our platinum partner is Jansen. Our gold partners are Genentech and Spark Therapeutics. Our silver partner and keynote underwriter is AGTC. Our bronze partners are Apellis, Two Blind Brothers, and REGENXBIO. These partners are essential to the success of this great conference. We hope to see many of you there in June.

Corporate sponsorships are, are also vital in supporting the foundation's ongoing programs and initiatives throughout the year. We recently announced that Spark Therapeutics is our first ever National VisionWalk sponsor. Since the first VisionWalk in the spring of 2006, our Vision Walks have raised more than \$60 million to fund site saving research. The VisionWalks are special community building events that bring people together to raise awareness and funds to support our mission. This past fall, we hosted 15 in-person VisionWalks plus our national, virtual VisionWalk, which collectively raised more than \$1.6 million. This spring there are 21 walks taking place. We expect those to drive more than 2 million in donations.

I'd also like to highlight two new Gold Outreach partners, Alnylam and Ocugen. Alnylam is new to our field and plans to initiate a Phase 3 program in Stargardt disease late in this calendar year. Ocugen recently initiated a first in human trial of its OCU400 in retinitis pigmentosa associated with NR2E3 and RHO mutations. OCU400 as the potential to benefit a broader group of RP patients as well. We greatly appreciate Alnylam and Ocugen strong support of our programs. We look forward to the data from these trials.

In addition to our core fundraising events, we continue to develop new and innovative approaches to raise additional funds for research. In March, we hosted our second Hope from Home, A United Night to Save Sight. It was quite a terrific evening with entertainment from our MC, Wayne Brady, great auction items and the opportunity to connect with others through our live party rooms. That was all while supporting the mission of the Foundation Fighting Blindness and all from the comfort of our participants' homes.

We want to thank the 400 plus Hope from Home attendees who joined us for this great event, which raised more than half a million dollars for our mission.

We also just wrapped up our first ever 250-mile cycling challenge fundraiser on Facebook. In a Facebook challenge, participants are tasked with completing a specific activity like biking for 250 miles over defined time periods, such as one month. While doing so, they raised funds from their friends and family members using a Facebook fundraiser. For our Facebook challenge, there were more than 620 participants who joined the event's Facebook group to connect with other participants, donate to each other's fundraisers and log in and share progress updates while learning about local resources, such as chapters and more. This online fundraiser reached new supporters of the Foundation, presented unique opportunities for community engagement and also provided a new source of funds for the foundation, generating more than \$38,000.

I'd like to wrap up my comments today with our financial summary. The Foundation, as you recall, operates on a fiscal year that runs from July to June. I'll report on our financials through March. For the first nine months of fiscal 2022, our unrestricted fundraising revenue was \$21.5 million, against operating expenses of \$11.5 million for a net fundraising surplus of \$10 million. We're tracking positively relative to our overall budget plan for this fiscal year, which includes targeted revenue of \$27 million against operating expenses of \$18 million. Importantly, the Foundation expects to spend roughly \$20 million this fiscal year on research projects that we believe will lead to preventions treatments and cures for people affected by retinal degenerative diseases.

On that note, my colleague, Dr. Amy Laster is joining us today to share a summary of the newly announced research awards that will be funding starting in 2022. Amy, go right ahead.

**Dr. Amy Laster, VP, Science & Awards Programs:**

Thank you, Peter. The foundation funds a diverse portfolio of emergent therapies to address the entire spectrum of inherited diseases and dry AMD for all patients affected, regardless of the mutated gene causing their disease or the severity of vision loss.

We are currently funding 86 active grants that are being conducted by nearly 100 research investigators at 65 institutions, eye hospitals and universities. To date, for fiscal year 2022, we have awarded 10 new research grants, totaling an investment of more than \$7 million in funding through our Translational Research Acceleration Program, you may hear us refer to it as TRAP, the Free Family Foundation, age-related macular degeneration or AMD program, and the Diana Davis Spencer Clinical Research Fellowship Program. We also have several other research program awards that we will be announcing in coming months, so we're not done yet.

The level of interest and need for funding remains high. In total for the three programs I've already mentioned, we received more than 75 pre-proposals, or letters of intent, that led to 25 full applications. Of these, they resulted in the 10 new grants I've mentioned. Now, these were selected after a rigorous review process conducted by the Foundation's Scientific Advisory Board, which is comprised of more than 60 of the world's leading retinal scientists and clinicians.

I'd like to summarize these awards and the range of research topics that are encompassed. Our Translational Research Acceleration Program is targeted to accelerate the movement of particularly promising preclinical research towards the clinic. This year we receive applications across all of our therapeutic research priority areas, including novel medical therapies or pharmaceuticals, genetic technologies, and regenerative medicine or cell-based therapies. This year's new cohort of TRAP awards includes three novel medical therapy projects. One addresses new targets for AMD therapies. Another is developing a mutation agnostic drug therapy for IRDs. The third seeks to prove that, yet still another mutation agnostic drug, is effective in preserving cone loss in retinitis pigmentosa.

Additionally, we awarded two regenerative medicine projects. One will develop cell transplantation technology for the replacement of retinal pigment epithelial, or RPE, and photoreceptor cells in retinal degenerative diseases, independent of the underlying cause. The second will explore how to replace lost photoreceptors and restore their function by activating intrinsic regeneration capabilities. In addition to these programs, we also awarded a multi-investigator collaborative award called a TRAP Program Project Award. This is to address causes and treatment strategies of inflammation that may be associated with gene therapies.



The Free Family Foundation AMD initiative in collaboration with the Foundation is funding research to understand the disease mechanisms that cause the transition from aging to early dry age-related macular degeneration, or AMD. After reviewing this year's applications, our AMD scientific advisory subcommittee recommended making an award to a team that's working on developing and testing a gene therapy for dry AMD. Their goal is to restore compliment regulation to the site of disease initiation, the retinal pigment epithelial choroid interface, using viral vectors, similar to those in current clinical testing for treating retinal dystrophies. The Diana Davis Spencer Clinical Research Fellowship Award Program provides funding for medical doctors in clinical fellowships, examining patients with inherited retinal degenerations. The program goal is to increase the number of clinician scientists with expertise and a commitment to provide clinical care to patients with inherited retinal disease. This program also prepares burgeoning doctors for careers in academic medicine and provides critical training in an environment that fosters research to develop preventions treatments and cures for retinal degenerations.

We have awarded three new grants for this year, which span research focusing on clinical imaging to develop new outcome measures of rod function, identifying elusive genes, and finally, the development of gene therapy strategies for mutations in PRPF31 associated retinal diseases. It is truly exciting to witness the innovation, new developments and progress across our entire range of research funding. We are dedicated to supporting the researchers and institutions who are advancing many promising therapeutic modalities in development, including gene therapies and gene editing that we'll hear about later from Dr. Pennesi, cell-based therapies and pharmaceuticals. The awards we are making this year will fuel our future achievements and our ability to ultimately help everyone diagnosed with inherited retinal diseases and dry AMD, regardless of their gene mutation and degree of vision loss.

I am now pleased to hand the call over to our CEO, Dr. Ben Yerxa.

**Dr. Ben Yerxa, Chief Executive Officer:**

Thank you, Amy.

The continued expansion of our research funding is really our top priority throughout the year. It's more than just a once-a-year occurrence. We've had multiple new research commitments to announce during the year on our Insights Forum Calls. That is the fuel that motivates our team and inspires our community.

The dedication and enthusiasm of researchers was evident last week at the annual meeting of the Association for Research in Vision and Ophthalmology, also known as ARVO. In conjunction with this major conference, the Foundation and Oregon Health and Science University (OHSU) hosted our Seventh Annual Retinal Cell and Gene Therapy Innovation Summit. Their representatives from biotech and pharmaceutical industries came together with physicians and scientists to discuss the rapidly emerging ocular gene and cell therapies, and to strategize on how to move the most advanced retinal disease therapy options forward. The Summit featured presentations by more than 40 leading retinal disease experts on a range of topics, including patient care and natural history, preclinical and clinical gene therapy, , antisense oligonucleotide therapy, and preclinical and clinical cell based therapy.

The program was anchored by remarks from Drs. Renee Ryals and Paul Yang, of OHSU Casey Eye Institute, and a keynote address on AAV gene therapy & ocular inflammation by Dr. Dominik Fischer of the University of Oxford and University of Tuebingen. We greatly appreciate the support and participation of our industry's leaders in the Summit, in particular our presenting event sponsor, ProQR.

I'd like to highlight an important upcoming meeting that is a unique form of a public forum attended by representatives of the U.S. FDA. The session is an Externally-Led Patient Focused Drug Development meeting for X-Linked Retinitis Pigmentosa, XLRP. This patient-focused XLRP meeting will be held on June 7, 2022.

The goal of the meeting is to educate FDA staff and other key stakeholders such as biotech and pharmaceutical companies about what is like to live with XLRP and current approaches to management or treatment.

This includes perspectives from both affected individuals, as well as caregivers and family members of affected individuals. The FDA staff may then use this information when reviewing new clinical trials or new drug applications for XLRP. The foundation recently hosted an educational webinar about the upcoming meeting and the FDA drug review process. If you want to learn more about this topic, the replay is available on our website, [www.fightingblindness.org](http://www.fightingblindness.org).

During our last Insights Forum, we shared an overview of a series of natural history studies designed to increase our understanding of disease progression and inform the design of future clinical trials in patient recruitment. There have been several new developments regarding these studies that I want to highlight briefly today. At last week's ARVO conference, there were three new scientific presentations made, based on data from the RUSH2A study, which focused on individuals with retinal degenerations caused by mutations in the USH2A gene. The genetic mutation is a leading cause of Usher Syndrome Type 2A and autosomal recessive retinitis pigmentosa. The four-year study was launched in 2017 and completed enrollment in 2019.

We recently completed enrollment in the Pro-EYS Study, which is focused on retinal degenerations caused by a mutation in the EYS gene, one of the more common causes of autosomal recessive RP. This ongoing four-year study, which was launched in late 2019, is evaluating a variety of clinical measures with a goal of identifying those measures that are most useful to apply in future clinical trials to show if a therapy is working.

And finally, I'm pleased to announce that our Uni-Rare Study is expected to launch patient recruitment in Q4 of 2022. Our previous natural history studies have focused on inherited retinal degenerations associated with a single gene. The Uni-Rare study will include individuals with many different disease-causing genes, including those that are considered very rare. This study will provide a baseline to identify patients with many types of mutations.

We're really grateful to the study participants, sites and clinicians who support these natural history studies. This foundational research helps to inform the development of new approaches in treating and potentially preventing inherited retinal diseases.

We have one of the leaders in novel RD research with us on the call today. I'm really pleased to welcome Dr. Mark Pennesi, Professor of Ophthalmology at Oregon Health and Science University and the Chief of Ophthalmic Genetics Division at the KCI Institute. He's also a key member of the Foundation's Scientific Advisory Board. Dr. Pennesi is a clinician scientist with a passion for developing novel therapeutic regimens for inherited retinal diseases. He has helped propel the KCI Institute into a leader in novel therapies for inherited retinal disease. He's the primary investigator on numerous clinical trials, including gene augmentation therapy for numerous types of inherited retinal diseases. He has a combined MD PhD from Baylor College of Medicine and an undergraduate degree from University of Pennsylvania. Dr. Pennesi has won numerous awards throughout his career, including the Foundation's Career Development award. While he could present on a million different topics today, Dr. Pennesi is going to talk about the use of gene editing in inherited retinal diseases, such as X-linked retinoschisis, and other topics.

Thanks for joining us today, Mark. Please go ahead.

### **Dr. Mark Pennesi, Oregon Health & Science University**

Thank you, Ben. It's really a pleasure to be here with my FFB family. I see some of my patients on the chat box, so hello. I'm really excited today to talk a little bit about gene editing, which is a rather new technology.

I'd like to start off first by starting at a very high level and talking about what makes gene editing different from gene replacement or gene augmentation therapy, which is what we've been using for the past 10 or 15 years, in an attempt to treat retinal degenerations. Right now, we have one approved treatment for inherited retinal degenerations and that's voretigene neparvovec or LUXTURN A. That is a gene replacement therapy for a gene called RP65.

Let's kind of start at a high level. The way I like to think about inherited retinal dystrophies and genetics is that if you think about our genome, it's a bit like a library of cookbooks. We have 23 different chromosomes, so you can kind of imagine 23 different bookshelves.

Each of those bookshelves has a cookbook, which is a gene, and that cookbook has the instructions in the gene of how to make a particular protein. It might be RP65 or USH2A, or SUP290. You can imagine a mutation to be an error in that cookbook. Some mutations are very small, they might be a single letter. Other mutations might be very large. It might be like ripping a page out of the book.

A mutation can have a big impact. If we think about, if we pull one of those books off ... Let's say it's a recipe to make a cake. The instructions are to put in two cups of sugar. Well, if we change that, a single letter, instead of a two it's now a nine, you're going to have nine cups of sugar and that's going to be a really sweet cake. Similarly, if we take out an ingredient, delete one of the words, we might be missing an ingredient. There are many different mutations. With gene replacement, essentially what's happening is, usually, we have a protein that's not being made. It's almost like you're missing the entire cookbook and you can't make that particular protein. With gene replacement, we're putting in a new copy of the gene. It's sort of like coming in and putting in a new copy of the cookbook. That works very well in certain diseases. It works very well when the gene is very small and we can deliver it within a virus such as an AAV virus.

Many genes are, are too big. The cookbook is too big to fit into that virus. We just don't have a way of delivering those large genes. Rather than taking the approach of trying to put in a whole new cookbook, what we really want to try to do is go in and fix the mutation itself. You can imagine a recipe where maybe the mutation is in the form of an extra ingredient. Now, in addition to putting some sugar in your cake, there's a line that says put in salt and that shouldn't be there. What if we could go in with an exacto knife and just sort of cut out that additional ingredient. That's sort of how gene editing works. What it lets us do is, it lets us go in and make little cuts in the DNA and take out mutations that are not supposed to be there.

For example, we're looking at a disease, leber congenital amaurosis, that's caused by mutations in a gene called C-E-P 290 or CEP20. This is a really big gene. It won't fit into your traditional gene replacement vectors. There's a common mutation that basically inserts a little sequence in the gene that creates a stop sign, such that the recipe gets cut off and the protein never gets made. What if we could go in and sort of cut out that little stop sign?

What we can do is we can design these little molecular scissors that target that stop sign, go in, cut it out. From that point, the protein will get made. It's sort of like restoring the ability of the cell to make the protein. That is a gene editing approach.

There are more advanced forms of gene editing, where we're not just taking an exacto knife and cutting something out, but where we can go in almost like a Word editor and go in and delete, and then replace the mistake. That'll be very powerful in the future when you have a single letter type of mutation where we might actually be able to go in and sort of cut and paste errors. That's something called prime editing, which is a new technology. Still hasn't really been tested out.

The really exciting thing is when it comes to gene editing, using CRISPR Cas, which is a bacterial set of proteins that we can use to make these little DNA cuts, we've actually started treating patients. There has been a trial sponsored by Editas. We have actually now treated a number of patients with this gene editing. This is still very early. This is a Phase 1/2 trial. We're starting with very, very advanced patients. Patients who have hand motion or count finger vision. What we're able to do is actually show that a couple of these patients have had an improvement in their sensitivity to light. One has even had an improvement in their visual acuity, after performing this gene editing. That's very exciting.

Now, I have to caution you, this is still very, very early data. We are still going through and doing dose escalations. We start at very low doses of the gene editing therapy, and then we slowly increase it. Thus far, the trial has completed dose escalation. We're actually now treating children. That's very exciting because we think that if we can perform the gene editing at a younger age, we might actually be able to restore more vision. This is very early, but the fact is that we're doing this today in people and this technology will continue to evolve. This is still the very first attempt and version 1.0, but there are even more advanced forms of this gene editing.

What's the downside of gene editing, as compared to gene replacement? Well, one downside of gene editing is that you have to make it to a specific mutation. Some genes might have hundreds of different mutations in them and the gene editing's only going to work for that specific mutation.

Unlike with gene replacement, that often will work for many different mutations, because we're just putting in a new copy. Gene editing may not be as scalable, because it's very specific. Many genes have common mutations. If we target those common mutations, we can get a large percentage of the population of patients with that particular problem.

That's just kind of a 30,000 foot overview. I think this is a very exciting technology. We're going to see it continue to evolve and it really is going to open up the ability to treat many more genes than we could before. I'll stop there and turn it back.

**Jason Menzo, President and Chief Operating Officer:**

Awesome. Thank you so much, Mark, not only for providing that terrific overview of gene editing, but also for making time to be on this call today. I know you're very busy. You're certainly one of the busiest clinicians in this space. I know, on behalf of the Foundation, and all of our attendees today, we appreciate you carving out time and again for that terrific overview.

It's about 20 minutes left in our time together, which is great, because it gives us plenty of time to start to cover off on the many questions that we've received. So far, we have somewhere in the neighborhood of 20 questions. Of course, if you have questions that you've not yet asked, we're going to have instructions here in a second on how to ask those.

Chris, I'm going to ask if you could please reread the instructions on how our attendees can ask their questions.

**Chris Adams, VP, Marketing & Communications:**

Sure. Thanks, Jason. Again, there are several methods for asking your questions. The first, you may access the Q and A and chat features featured at the bottom of the Zoom control bar and then type in your questions. Secondly, if you have questions, feel free to email us at [info@fightingblindness.org](mailto:info@fightingblindness.org).

Again, that is [info@fightingblindness.org](mailto:info@fightingblindness.org). Please note that if there are questions that we aren't able to answer today, we will follow up with you directly with those answers to your questions. Jason?

**Jason Menzo, President and Chief Operating Officer:**

Thank you so much, Chris. While we're compiling our questions, I'd like to let everyone know that in addition to our speakers, which of course were Ben Yerxa, Peter Ginsberg, Amy Laster, Chris Adams, Dr. Mark Pennesi, we're also joined by our Chief Scientific Officer, Dr. Claire Gelfman, who will help field some of our questions. Like I said, we have 20 some odd questions that have been chatted and we're likely not to get to all of them. As Chris had mentioned, anything that we don't get to, we will follow up with every single question offline, if needed.

The first question I wanted to address though, there were several questions about VISIONS, which was one of the highlights of our presentation earlier today.

The question is, "Are the presentations from VISIONS going to be available if you're unable to attend live and in-person?" Our hope is that as many people join as possible in-person in Florida, however, there will be certain elements of the program that will be streamed live. There will be certain elements that will be available on demand afterwards. We also will provide audio recordings and full recap of VISIONS. While we hope that everyone that is able to attend live does, if you are unable to attend, for whatever reason, there will be opportunities to still get exposed to the information that we present at VISIONS.

The next question I'm going to direct to you Ben. A couple months ago, we announced the newest company funded by the RD Fund, Opus Genetics, and one of their early programs is for LCA5. Wondering if you could speak a little bit about that program and what the status is?



**Dr. Ben Yerxa, Chief Executive Officer:**

LCA5 is actually the lead program for Opus Genetics right now. The company has said that it plans to file the IND in the U.S. around midyear with a clinical start before the end of the calendar year. So stay tuned.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Ben. Dr. Pennesi, I'm going to come back to you. We had a question that was actually emailed before the session today about achromatopsia. Curious if you could just provide an overview of the landscape for achromatopsia specifically, any new trials, et cetera.

**Dr. Mark Pennesi, Oregon Health & Science University**

There were actually a number of presentations at the recent ARVO meeting and there are multiple Phase 1/2 trials in achromatopsia, both in CMGB3 and CMGA3 mutations. I think there actually is some exciting news. One specifically would be the AGTC Phase 1/2 trial for patients with CMGB3 mutations. They've done gene replacement therapy now in a number of patients and they have seen an improvement in light sensitivity in many of those patients, as well as when you look at visual fields using a special kind of stimulus. If you use a red stimulus, many times, patients with achromatopsia really are insensitive to red light. What we're seeing after we treat those patients is they can actually start to see the red light on the visual field. That's really interesting and does suggest that there is some biological effect going on to the gene therapy.

I think the issue with achromatopsia is that in terms of restoring things like visual acuity, we probably have to treat at a very young age because there may be a critical window of brain development. Treating adults, I think, we might be able to help things like the photosensitivity, but we may not be able to improve things like the visual acuity.

Hopefully, if we can treat young enough maybe we can actually improve those. That's something that we're going to need to explore in a Phase 3 trial. I'll stop there.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Mark. Ben, I'm going to come back to you. Another question about a different specific inherited retinal disease, Best disease. I know that there's some information in the public markets about a program for Best disease. Maybe you can speak a little bit to what's happening in that space.

**Dr. Ben Yerxa, Chief Executive Officer:**

Not a whole lot of extra information. We are aware of a program that we funded at the University of Pennsylvania that was licensed by Iveric Bio. They progressed that program up to a pre-IND level. They have said, publicly, that they plan to partner that program. We'll have to wait and see what Iveric decides to do with that program. We're tracking it at the Foundation level. We think it's really good science and hope someone will pick it up and bring it forward.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Ben. Todd, I'm going to direct this next question to you. An individual chatted in that they were diagnosed with retinitis pigmentosa several years ago. They're having a meeting with a genetic counselor next week. The question really is, what happens if it doesn't reveal the specific gene mutation? Questions like how often should they retest? Right after this question, I'm going to shift to Claire for another question that's come up about some of our funding for elusive gene program. How we fund looking for genes that have not yet been identified.

Todd, let's have you start by addressing the first part of the question, then Claire will go to you after.

**Dr. Todd Durham, Senior Vice President of Clinical & Outcomes Research:**

Hi, this is Todd Durham. It is true, even with the best commercial clinical panels that we have today, sometimes, maybe up to 20% of cases, we won't find the causative gene responsible for your RP. I would encourage you to have a lengthy and fulsome conversation with that genetic counselor. He or she will be able to key you into the available research and what's in the pipeline. As far as the Foundation is concerned, there are a number of therapeutic approaches that are in the clinical trial pipeline. Things like antioxidants, like NAC and NACA. There's also an approach called optogenetics that uses genetic therapy to deliver oxins to the target cells, which may be more amenable to those with more advanced vision loss. Sparing Vision, another one of the Foundation's portfolio companies has developed a broad derived cone viability factor, which also helps prevent or reduce oxidative stress and protect the photoreceptors from further degeneration.

Those are some options in the clinical trial pipeline. We really are helpful about these approaches, because as you're a question indicates, there are a lot of people who would benefit from gene agnostic approaches to therapy. Then I'll turn the rest over then to Claire.

**Dr. Claire Gelfman, Chief Scientific Officer:**

Thank you, Todd. This is Claire Gelfman. Thank you for that overview of those agnostic approaches.

With that though, we are still very interested in helping move forward this whole idea of elusive beings. We actually have four major research projects, currently in progress, that are specifically targeting the identification of previously unrecognized genetic causes of inherited retinal diseases, which we refer to as these elusive genes.

As Todd mentioned, the specific genetic cause remains elusive actually up to half of known IRDs in the IRD population with autosomal recessive diseases being the most challenging. As these elusive genes are typically thought of as genes not previously identified as being associated with an IRD. Research funded by our Elusive Genes Initiative, revealing that some of these elusive cases, they can be attributed to these pathological structural changes in the DNA, in the genome, such as a rearrangement, a duplication, or even a translocation, genes already known to be implicated in inherited retinal diseases. Addition to these technical challenges, these technical weaknesses, existing technologies that are used in traditional genetic analysis. The findings really highlight the importance of continuing to fund these adapting genetic testing platforms, as these new mechanisms of disease are identified.

**Jason Menzo, President and Chief Operating Officer:**

Thank you so much, Claire. That was very good. I want to just emphasize that, as an organization, we're funding, not just specific programs specific to the genes and as a field, not just to the Foundation, but the field. There's so many, we use this analogy, shots on goal across a variety of different approaches, whether it be specific to the gene or gene agnostic as Todd and Claire just mentioned. While genetic testing is super important, the My Retina Tracker program is a really important initiative to help advance the field. We have really many things from a strategic perspective, both in identifying genes that have not yet been identified, but also advancing treatments that potentially could work across the spectrum, regardless of the gene mutation. Super important.

Let's shift, again, to Ben. There was a question about a particular gene that has also been publicly disclosed as being one of interest for Opus Genetics, and that's NMNAT1. If it's possible, just to speak about that program at a high level. This particular question may be a little technical, we may want to follow up offline, but it's about the model in particular that is used in the preclinical work. To whatever degree you can answer that and we can follow up with more detail offline.

**Dr. Ben Yerxa, Chief Executive Officer:**

Thanks, Jason. For the NMNAT1, it's a program licensed to Opus Genetics from Eric Pierce's lab at Harvard Mass Eye and Ear. It was based on the excitement from the paper that was published in the mouse model that showed both some structure and functional improvements after gene therapy. That's about all I can say on this particular forum, but we'd be happy to follow up with some more details later.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Ben. We've got just about 10 minutes left. We're going to tackle a couple more questions. Dr. Pennesi, I want to ask one to you that was chatted in, as well, which is really about the field as it relates to Stargardt. This is obviously ABCA4 is a very common mutation in the whole IRD landscape, and obviously Stargardt represents a big percentage of the IRD community. Can you speak to what's happening in the field, clinical and maybe a little bit about preclinical work, that's exciting from your perspective for Stargardt.

**Dr. Mark Pennesi, Oregon Health & Science University**

I think Stargardt is one of the diseases where we have a lot of irons in the fire right now. There are many different potential avenues for treatment. Gene therapy is certainly one option and there have been trials in the past using lentivirus to deliver the ABCA4 gene. Those were not largely effective, but there are alternative approaches to doing this, maybe using dual vector AAV or lipid nanoparticles, or other ways of delivering larger genes. I think, certainly, that's going to be one approach. Then there's also a variety of drug approaches and primarily related to vitamin A metabolism. Slowing down the metabolism of the rod photoreceptors, so they're not making as much of the toxic byproducts.

That can be done either by limiting vitamin A metabolism. There are a variety of drugs and companies that are working on that approach.

There's a company working on a form of vitamin A that is deuterated or kind of hardened so that it doesn't form the toxic byproducts. There was some very interesting data at the recent ARVO meeting suggesting that that drug may slow down progression. Finally, there's also approaches that are anti-inflammatory in nature, looking at complement factor and blocking complement factor. There really are four or five different trials underway, or soon to be underway, for that disease. We're going to have to wait though and see what the data actually shows and to see which of these approaches are effective.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Mark. We've been talking quite a bit about science and research and genetic testing, et cetera. There are a couple questions about the business side. I use that term intentionally, because it's really about the adjacent, for-profit entities that are also helping to mobilize resources to advance our mission. Peter, maybe you could speak a little bit to how we're mobilizing corporate sponsors, other entities that are adjacent to helping us solve our mission.

**Peter Ginsberg, EVP, Corporate Development and Chief Business Officer:**

We have so many important stakeholders here at the Foundation. Of course, patients are first and then clinicians, researchers and the companies running these clinical trials. Many different sets of important stakeholders. The companies that you've referred to, play a very important role in bringing these new therapeutics forward. The Foundation is supportive of that effort and on the flip side, the corporations support the Foundation. We have a dozen corporate outreach partners and about the same number of corporations that fund our My Retina Tracker registry and genetic testing efforts. These companies play a very important role in helping us to expand our programs and to drive them forward.

We continue to seek additional partners among biopharmaceuticals companies, contract research organizations, and others in our field. We also have a new, and I think quite exciting, endeavor to bring in more corporate partners outside of our biopharmaceuticals field. Other technology companies, transportation companies, other industrial organizations that might have an interest in helping to fund our research and other programs. A lot of activity on that front. That's a very important endeavor for us.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Peter. I would just request anyone that's on the call today that has access to a relationship with, or just a path for introductions into any local or Fortune 500 companies that you'd like to make an introduction to the Foundation. Please reach out to us at [info@fightingblindness.org](mailto:info@fightingblindness.org). It's super important to have those personal connections to open doors. We have just a couple minutes left. I'm going to ask three final questions. Although one that just got chatted in, I think we should address today too, which is with relation to vitamin A and Stargardt. We'll get to that in a minute.

Amy and then Claire, and then Todd, the questions are ... Amy can you briefly provide an overview of how does one inherit gene mutation for an IRD or maybe just a brief overview of inheritance patterns. Claire, I'm going to ask you then to talk a little bit about how does one participate in a clinical trial or find out about them. Then Todd, a little deeper on natural history studies. Amy, we'll start with you.

**Dr. Amy Laster, VP, Science & Awards Programs:**

Heredity is really based on three major genetic disease inheritance patterns. I'll highlight those. Autosomal dominant, this is a disease in which you inherit one copy of a gene with a mutation from an affected parent. It's likely that the affected parent typically knows that they have the disease and have some of the related symptoms, while the other parent usually is not affected, or even carry that particular mutation.

With these types of diseases or dominant diseases, it's about a 50% chance that those diseases will be passed on the child. Now, with recessive disease, the child must inherit a mutation in the gene from both parents. With these conditions, each parent has one of the mutated copies and a normal copy. Again, the child inherits the mutated copy from their each one of their parents. With the recessive disease, there's about a 25% chance that the child will be affected and about a 50% chance that they may be a carrier of the disease, but unaffected.

Then the last type of inheritance pattern is X-linked diseases. They're really more complicated than the others, because the gender of both the parents and their children often determine whether or not the gene is passed down. Men have an X and a Y chromosome. Whereas, women have two X chromosomes. The mother passes an X down to their sons. Daughters, they don't get affected because they have a healthy X chromosome. However, women can have mild vision loss or even suffer from very severe vision loss if they have an X-linked retinal disease. Typically, it is the son that inherits it. There's about a 50% chance that the son will be affected by an X-linked disease.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Amy. I'm going to go out of order. Just because I know we're right at time. I want to make sure we address this before folks hop off. There's a question about vitamin A, if one has Stargardt and there was just some questions actually we received just in the last couple days about that. I want to make sure we address that. Claire. Can I ask you to just, at a high level, speak to that point? If one has Stargardt, is vitamin A recommended or what should one do?

**Dr. Claire Gelfman, Chief Scientific Officer:**

Thanks, Jason. This is Claire Gelfman. The short answer is no, it's not recommended for someone who is affected with Stargardt to take any form of vitamin A.



The reason for this, as we were hearing earlier what happens in Stargardt, when a person has a mutation in the ABCA4 gene, is that the visual cycle ... Think of it as being overactive in that there is a buildup of toxic byproducts due to the presence of vitamin A. You wouldn't want to exacerbate that process any more than it already is exacerbated. Again, you should speak to your individual physician about questions like this, but, at very high level, it is not recommended for individuals with mutations in ABCA4, who have been diagnosed with Stargardt, to do any additional vitamin A or beta-keratin supplementation in their diet.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Claire. Why don't you briefly speak about how does one find out about clinical trials? How does one get involved in clinical trials? Then Todd, you'll have the last word to talk a little bit about natural history studies to close things out.

**Dr. Claire Gelfman, Chief Scientific Officer:**

Thanks Jason. This is Claire again. I think it's a great segue into talking a little bit about a wonderful resource that we offer for all affected individuals. When you go to your ophthalmologist and get a diagnosis of an IRD, we actually offer free genetic testing for anyone who gets that clinical piece of information from your physician. Your physician will place an order for testing that's free of charge to the patient. Then along with receiving those test results, we also offer free genetic counseling. This is through partner partnerships with both Blueprint Genetics, and Informed DNA. That's really important, because it's one thing to get testing and get this information in front of you, but sometimes it's a difficult to really go through it all. Counseling can really help interpret that information.

Then all that information then gets deposited into our Registry. Our Registry is 20,000 strong. The reason I bring this up in answer to your question, Jason, is because our Registry is a source of individuals for clinical trial enrollment that companies will use in order to enroll for any clinical trial, for an inherited retinal disease. By virtue of being in our Registry, you are putting yourself in a position to be called upon for participation in a clinical trial.

In order to learn about other clinical trials that are going to be relevant to you, there is a website called [clinicaltrials.gov](http://clinicaltrials.gov), where you can enter your specific mutation or your specific diagnosis. What will pop up will be all clinical trials in the space and companies who are working on it. You can contact those companies directly. You can speak to your physician about it. Those are just three different ways to ensure learning about an enrollment in clinical trials for your diagnosis.

**Jason Menzo, President and Chief Operating Officer:**

Thank you, Claire. Todd, finally, there were a couple questions about natural history studies. Someone referenced natural history studies early in the presentation. Maybe you can just speak a little bit deeper about what they are, why they're important and how does one find out about them?

**Dr. Todd Durham, Senior Vice President of Clinical & Outcomes Research:**

Hi, everyone. This is Todd Durham, again. As you know, and as Ben Yerxa mentioned, we conduct our own natural history studies of inherited retinal diseases. The reason why these are important is we don't necessarily have very comprehensive, detailed information about how these diseases progress in the absence of therapy. In order to successfully develop a new treatment for many of these conditions, we need to understand very well the measures of visual function and understand the anatomy of the retina. These can be important tools, ways to mark any benefits that are conveyed by an investigational therapy. Without detailed information like this, we'll rely on some assumptions about how much these vary from person to person, whether certain individuals are more prone to say, faster acceleration.

We really want to identify the ideal target population in a clinical trial and understand how large that study needs to be and how long we need to follow people.

Understanding these metrics in the absence of therapy, helps us and our clinical trial partners develop trials that are more likely to be successful. That's the importance of those. If you have any of the conditions that we are studying, in our studies, I'm always happy to field your email and direct you to our coordinating center who manages the day-to-day activities of these studies and see if you may be eligible to participate.

**Jason Menzo, President and Chief Operating Officer:**

Well, admittedly, I fell short today because it's 12:05 here on the East Coast. Normally, we cut these right off on time. We're five minutes over. I'm looking at the Q and A and there are 55 questions that came in, of which we only were able to get to a very small percentage of them. You have our word that we'll be following up with any questions that went unanswered on the call today.

Also, just one final comment. For those who are new to our community. There's so many that have been chatted in, stories about wife or husband recently diagnosed, brother, sister, daughter, son, father, mother, recently diagnosed. Welcome to the community. You're part of a very strong and robust global community in the inherited retinal disease space. The Foundation Fighting Blindness is very happy to be a leader in advancing potential treatments and cures for the wide range of inherited retinal diseases.

You can always learn more about who we are, what we're doing, both from a community engagement and fundraising perspective, but also from an education, genetic testing, advancements of research perspective. All of this is available at our website [fightingblindness.org](http://fightingblindness.org). Also, you can reach out to us. We've got people all over the country, that'd be happy to connect with any of you, individually, both staff, as well as volunteers. Our chapters are very strong all over the country. You can contact us at [info@fightingblindness.org](mailto:info@fightingblindness.org). Thank you all for joining us today. I think it was a great discussion. Be sure to check out, not only the website, but our Facebook page. We're on Twitter. We're on LinkedIn. We're on Instagram. We try to get as much of our information out into the public as possible. Thank you. Have a great rest of the day. We'll see you in a couple months at the next Insights Forum. Thank you.